REMARKS/ARGUMENTS

Claims 1 and 30 remain in the application. Reconsideration of this application, in view of these remarks, is respectfully requested.

Claims 1 and 30 stand rejected under 35 U. S. C. §103(a) as being unpatentable over Schwartz (U. S. 2003/0013857 A1). This rejection is respectfully traversed for the following reasons.

Schwartz, U.S. Patent Application Publication 2003/0013857 A1 (hereinafter "Schwartz"), discloses modified solid supports that include solid supports that have been modified by reaction with a bifunctional reagent that possess a hydrazine or oxyamino group. These modified solid supports are useful in immobilization of biomolecules that possess or are modified to possess a carbonyl group. In one embodiment, aliphatic bifunctional hydrazide reagents are provided. See paragraph [0018] of Schwartz. These reagents include a cleavable bond for further manipulation. Cleavable bonds include, but are not limited to, acid cleavable, photocleavable and disulfide bonds. See paragraph [0109] in Schwartz.

Schwartz discloses a method of attaching a protein to a functionalized solid surface through a hydrazone linkage, wherein the protein is immobilized to a functionalized solid support via hydrazone bond formation. Schwartz discloses hydrazone bond formation as useful for conjugating biomolecules to other biomolecules and to fluorescent dyes. Schwartz discloses cleavage of the hydrazone bond to form useful products. However, Schwartz does not describe the preparation of conjugates comprising two macromolecules using conventional bifunctional reagents.

None of the conjugates described in Examples 12, 14, 16, 20 of Schwartz correspond to the conjugates of the present invention, which comprise a First Macromolecule and at least one Second Macromolecule, because the conjugates described in Schwartz include a hydrazone bond linking the First Macromolecule and the Second Macromolecule. The hydrazone bond has been described as being cleavable, both by Schwartz and the specification of the present application. It is clear from paragraphs [0057] and [0110] of the specification of the present application that the linker between the First Macromolecule and the solid is cleavable while the linker between the First Macromolecule and the at least one Second

Macromolecule is not cleavable. This conclusion is indisputable because if the bond between the First Macromolecule and the Second Macromolecule were cleavable, the conjugate would no longer exist after the complex comprising the First Macromolecule and the Second Macromolecule is detached from the solid support. Thus, it is clear that Schwartz teaches away from the method described herein because Schwartz calls for the cleavage of the First Macromolecule (protein) from the Second macromolecule (protein), which cleavage would destroy the conjugate. Moreover, both a cleavable linker and a non-cleavable linker are required in the method described herein, and Schwartz fails to disclose or suggest the use of a non-cleavable linker. In view of the foregoing, it is submitted that Schwartz does not render claims 1 and 30, as amended, obvious to one of ordinary skill in the art.

Upon a more detailed review of Schwartz, it can be seen that Schwartz describes methods for attaching a first macromolecule to a second macromolecule. See for example, paragraphs [0110], [0111], and [0112] of Schwartz. Paragraph [0110] of Schwartz describes the use of cleavable linkers to create a drug-antibody conjugate, which is cleaved by physiological processes following endocytosis. Schwartz also refers to the use of cleavable disulfide linkages to isolate receptors following covalent linking between a ligand and a receptor. Paragraph [0111] of Schwartz describes the use of bifunctional hydrazides to modify biomolecules or carriers in a single step. These modified aliphatic hydrazide molecules or carriers can be subsequently reacted with carbonyl containing biomolecules, drug, or other therapeutic or diagnostic reagent to form a hydrazone that can be cleaved following exposure to mild aqueous acid conditions. Paragraph [0112] of Schwartz describes that solid supports such as beads, chromatographic supports or surfaces are modified with aliphatic hydrazide reagents.

Schwartz also describes methods for attaching a chain of macromolecules to a surface. See, for example, paragraphs [0147], [0150], [0158], [0177], [0179], and EXAMPLES 6, 7, 8, 18, and 21 of Schwartz.

(a) Paragraph [0147] of Schwartz describes hydrazino modified beads for forming stable hydrazones when reacted with molecules possessing carbonyl groups.

(b) Paragraph [0150] of Schwartz describes hydrazine and oxyamino

silanes that are useful for modification of silica surfaces to generate hydrazine and oxyamino glass.

(c) Paragraph [0158] of Schwartz describes reagents to incorporate hydrazine and oxyamino groups on thiophilic metals, surfaces and particles.

(d) Paragraph [0177] of Schwartz describes that the reagent provided therein may be utilized to form crosslinks between a wide variety of molecules, including. for example, protein-protein conjugates (e.g., monoclonal antibody/enzyme conjugate) or protein-polymer conjugates (e.g., monoclonal antibody to a microtiter well surface).

(e) Paragraph [0179] of Schwartz describes immobilization of biomolecules to surfaces using a crosslinking couple by modifying the biomolecule with either a hydrazino, oxyamino, or a carbonyl moiety and contacting the modified biomolecule to a surface possessing its reactive partner, e.g., a hydrazino or oxyamino moiety for a carbonyl-modified biomolecule, or a carbonyl moiety for a hydrazino- or oxyamino-modified biomolecule.

(f) EXAMPLE 6 of Schwartz describes modification of glass surfaces by hydrazone-protected hydrazine silane reagent.

(g) EXAMPLE 7 of Schwartz describes prepration of 96 well plates to incorporate aromatic aldehyde moieties.

(h) EXAMPLE 8 of Schwartz describes preparation of 96 well plates to incorporate aromatic hydrazine moieties.

(i) EXAMPLE 18 of Schwartz describes a general procedure for the modification of gold particles with succinimidyl hydrazinium modification reagent.

(j) EXAMPLE 21 of Schwartz describes immobilization of horseradish peroxidase to hydrazine-modified plates.

However, Schwartz fails to disclose or suggest a multiple-step method that includes all of the steps of (1) linking a first macromolecules to a surface, (2) linking a second macromolecule to the first macromolecule, and (3) disrupting the link between the first macromolecule and the surface in order to free the conjugate comprising the first

macromolecule and the second macromolecule from the surface without disrupting the covalent bond existing between the First Macromolecule and the at least one Second Macromolecule. Accordingly, Schwartz does not disclose or suggest a method containing all of the steps of the method described and claimed in this application.

Although Schwartz provides a number of descriptions of conjugations between biomolecules and solid supports and although Schwartz also provides a number of descriptions of cleavable linkers, Schwartz does not disclose or suggest a method for carrying out the methods described in claims 1 and 30.

In view of the foregoing, it is submitted that claims 1 and 30, as amended, are in condition for allowance, and official Notice of Allowance is respectfully requested.

Attached to this AMENDMENT AND RESPONSE ACCOMPANYING REQUEST FOR CONTINUED EXAMINATION is the NOTICE OF IMPROPER REQUEST FOR CONTINUED EXAMINATION (RCE) that was mailed on March 31, 2008.

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Abbott Laboratories
D-377 AP6A-1
100 Abbott Park Road
Abbott Park, Illinois 60064-3500
Telephone: (847) 937-6182
Fax. No.: (847) 938-2623

Respectfully submitted,
John C. Russell

/David L. Weinstein/

David L. Weinstein
Registration No. 28, 128
Attorney for Applicants

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PAUL D. YASGER
ABBOTT LABORATORIES
100 ABBOTT PARK ROAD
DEPT. 377/AP6A
ABBOTT PARK, IL 60064-6008

Paper No.

Application No.:	**10/062,131**	**Date Mailed:**	**03/31/2008**
First Named Inventor:	Russell, John, C.	Examiner:	HAQ, SHAFIQUL
Attorney Docket No.:	6885.US.O1	Art Unit:	1641
Confirmation No.:	2508	Filing Date:	02/01/2002

Please find attached an Office communication concerning this application or proceeding.

Commissioner for Patents

PTO-90c (Rev.08-06)

KMW 4-4

NOTICE OF IMPROPER REQUEST FOR CONTINUED EXAMINATION (RCE)	Application No. 10/062,131	Applicant(s) RUSSELL, JOHN C.	
		Art Unit 1600	Date Mailed:

The request for continued examination (RCE) under 37 CFR 1.114 filed on 18 March, 2008 is improper for reason(s) indicated below:

1. ☐ Continued examination under 37 CFR 1.114 does not apply to an application for a design patent. Applicant may wish to consider filing a continuing application under 37 CFR 1.53(b) or a CPA under 37 CFR 1.53(d). An RCE cannot be treated as a CPA.

2. ☐ Continued examination under 37 CFR 1.114 does not apply to an application that was filed before June 8, 1995. Applicant may wish to consider filing a continuing application under 37 CFR 1.53(b).

3. ☐ Continued examination under 37 CFR 1.114 does not apply to an application unless prosecution in the application is closed. If the RCE was accompanied by a reply to a non-final Office action, the reply will be entered and considered under 37 CFR 1.111. If the RCE was not accompanied by a reply, the time period set forth in the last Office action continues to run from the mailing date of that action.

4. ☐ The request was not filed before payment of the issue fee, and no petition under 37 CFR 1.313 was granted. If this application has not yet issued as a patent, applicant may wish to consider filing either a petition under 37 CFR 1.313 to withdraw this application from issue, or a continuing application under 37 CFR 1.53(b).

5. ☐ The request was not filed before abandonment of the application. The application was abandoned, or proceedings terminated on _____. Applicant may wish to consider filing a petition under 37 CFR 1.137 to revive this abandoned application.

6. ☐ The request was not accompanied by the fee set forth in 37 CFR 1.17(e) as required by 37 CFR 1.114. Since the application is not under appeal, the time period set forth in the final Office action or notice of allowance continues to run from the mailing date of that action or notice.

7. ☒ The request was not accompanied by a submission as required by 37 CFR 1.114. Since theapplication is not under appeal, the time period set forth in the final Office action or notice of allowance continues to run from the mailing date of that action or notice.

Note: A continued prosecution application (CPA) under 37 CFR 1.53(d) cannot be filed in a utility or plant application. A CPA filed in a utility or plant application that has a filing date **on or after June 8, 1995** will be treated as an RCE under 37 CFR 1.114. The request for a CPA in the instant application, however, has been treated as an improper RCE for the reason(s) indicated above.

A copy of this Notice MUST be returned with the reply.

Direct any questions concerning this notice to

/GLORIA TRAMMELL/, Technology Center 1600

Telephone Number: (571)272-0561